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The Distinguished Legacy of Linda S. Birnbaum, an Environmental Health Champion

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The canon of environmental health luminaries would not be complete without including the life works of Linda S. Birnbaum, PhD, DABT, ATS. As the first woman and the first toxicologist to direct the National Institute of Environmental Health Sciences (NIEHS) and the National Toxicology Program (NTP), Dr. Birnbaum established and embarked upon an ambitious strategic plan for the Institute that continues to shape and support impactful research progress in both the intramural and extramural environmental health research communities. Throughout her 10-plus years as Director, Dr. Birnbaum has mobilized cross-disciplinary and collaborative efforts to support her vision of "One NIEHS." As she steps away from her official roles (but not from science), we, as members of her senior leadership team, have reflected upon and wish to pay tribute to her exemplary leadership and many accomplishments at and on behalf of the NIEHS. Accordingly, we highlight key areas in which Dr. Birnbaum stands out as a motivator, innovator, champion, and role model for us all.

Leader in Strategic Planning and Institute Initiatives

Dr. Birnbaum arrived at the NIEHS in 2009 with a bold vision for the Institute going forward. To gain support for this vision, she drew upon many years of both research and leadership experience in the U.S. Environmental Protection Agency (EPA) Office of Research and Development, where she had been Director of the Experimental Toxicology Division, Acting Director of the Human Studies Division, and Acting Associate Director for Health in the National Health and Environmental Effects Research Laboratory. Upon her arrival at the NIEHS, she engaged the leadership team and a broad set of internal and external stakeholders to develop integrated themes and goals for both the 2012–2017 and 2018–2023 Strategic Plans (https://www.niehs.nih.gov/about/strategicplan/index.cfm). Once the plans were in place, Dr. Birnbaum ensured that we lived them and worked together in the spirit and embodiment of One NIEHS.

Building on this shared strategic vision over the past decade, the NIEHS made major advances in environmental health science, established innovative scientific research programs, and added new research capabilities. The following stand out as key accomplishments achieved under Dr. Birnbaum's directorship: The NIEHS

- Reestablished the NTP as an independent intramural division within the NIEHS with a dedicated internal laboratory resource to enable timely and flexible response to contemporary issues.
- Established the NTP Office of Health Assessment and Translation to integrate data streams in the assessments of noncancer effects. The latter are now considered the preferred model for conducting hazard assessments.
- Shifted the scientific paradigm to emphasize the importance of examining the early life stages (preconception/pregnancy/early childhood) as a critically vulnerable period of exposure and susceptibility by *a*) strengthening and extending the NIEHS/EPA-funded Children's Centers and *b*) establishing a national network of exposure assessment laboratories with innovative grant infrastructure in the form of the Children's Health Exposure Analysis Resource and Human Health Exposure Analysis Resource (https://www.niehs.nih.gov/research/supported/exposure/chear/index.cfm).

Linda S. Birnbaum, Director of NIEHS 2009–2019

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- Advanced the innovative Tox21 collaboration by *a*) expanding the unique partnership of the NIEHS, National Center for Advancing Translational Sciences, and U.S. EPA to include the U.S. Food and Drug Administration; *b*) demonstrating that high-throughput robotic testing can produce high-quality results on thousands of test articles; *c*) expanding the chemical library to >10,000 compounds; *d*) continually expanding the portfolio of cell-based assays; and *e*) uniquely building a first-of-its-kind high-throughput transcriptomics capability. Tox21 is a major effort to support the move of toxicology from a fundamentally observational science to a predictive one—an evolution needed to meet the demands of a rapidly expanding exposome (https://ntp.niehs.nih.gov/results/tox21/index.html).
- Expanded research in the field of epigenetics across all of the science divisions at the Institute, thereby fostering the application of epigenetics to all aspects of environmental health.
- Promoted the concept of complex mixtures—shifting the paradigm from investigating one chemical agent at a time—through funding, workshops, and cross-divisional working groups.
- Developed and initiated a unique and innovative strategic plan for the Interagency Coordinating Committee for the Validation of Alternative Methods, which has significantly increased the pace of adopting new alternative methods (ICCVAM 2018).
- Developed new criteria for evaluating strength of the evidence for toxicological outcomes of studies on reproduction, development, and the immune system, which were first applied to NTP reports in 2019.
- Advanced toxicity testing by *a*) adding gestational and lactational exposures to all rat subchronic and chronic toxicity studies; *b*) prompting the NTP to evaluate genetic variability across "mousedom" with the use of the Collaborative Cross and explore the use of Diversity Outbred mice as a more relevant model for genetically diverse human populations; and *c*) pairing rodent studies with studies of human variability using nearly 200 chemicals in close to 1,000 lymphoblastoid cell lines from nine ethnic groups on five continents. As a result of these efforts, there is credible evidence that the usual uncertainty factors used to account for intraspecies variability may be inadequate.
- Expanded the clinical research capabilities of the NIEHS to investigate environmental effects on human health and disease and provide outreach and services to patients while also providing new opportunities for NIH partnerships with cutting-edge biomedical teams.
- Increased the NIEHS capabilities by investing in a new Neurobehavioral Core Laboratory and a new Cryo-electron Microscopy Core Laboratory. The latter was crucial for the formation of the Molecular Microscopy Consortium, a joint initiative with Duke and UNC-CH aimed at establishing this Nobel Prize winning technology into the region.
- Built future scientific capacity by hiring outstanding and diverse investigators in the areas of immunology, reproductive biology, epidemiology, biostatistics/computational biology, epigenetics, neuroscience, signal transduction, and clinical research.
- Strengthened the NIEHS Director's office in Bethesda, Maryland, to better engage with Congress, other NIH Institutes and Centers, White House committees, other federal partners, professional associations, and nongovernmental organizations.
- Developed the Global Environmental Health Program at the NIEHS to focus research, education, training, and research translation to "health problems that are related to environmental exposures and transcend national boundaries, with a goal of improving health for all people by reducing the environmental exposures that lead to avoidable disease, disabilities and deaths" (https://www.niehs.nih.gov/research/programs/geh/index.cfm).

Supporter of Emerging Issues and Disaster Research

Dr. Birnbaum recognized that the NIEHS could play a unique role in recognizing and calling attention to emerging environmental public health issues and then frame research needs and priorities around them. With her support and encouragement, the Institute initiated the NIH Disaster Research Response Program, becoming a driving force to further national and international capacity for timely disaster research and responses. For example, the NIEHS led trans-NIH research projects following the 2010 *Deepwater Horizon* oil spill (Kwok et al. 2017) and the 2014 West Virginia chemical spill (NIEHS 2016). "Both studies required effective coordination with scientists across NIH, and with the residents of affected areas," wrote Francis Collins in a farewell tribute to Dr. Birnbaum (NIH 2019).

Time-sensitive award mechanisms have allowed scientists to collect data in the field sooner than before when a disaster occurs. The NIEHS also has created new research centers; provided training, protocols, and other scientific resources; and supported workers and those impacted by these events. Through these efforts, the NIEHS programs and research community has contributed to specific disasters, including chemical spills, hurricanes, wildfires, and outbreaks of infectious disease such as Zika—and continues to do so.

Dr. Birnbaum's vision enabled the NIEHS to spearhead a variety of approaches to study emerging environmental threats and contaminants such as harmful algal blooms, bisphenol A [through the Consortium Linking Academic and Regulatory Insights on BPA Toxicity (CLARITY-BPA) program], per- and polyfluoroalkyl substances (PFASs), and epidemics such as the increase of chronic kidney disease of unknown origin.

Promoter of Research Translation and Knowledge Dissemination

Dr. Birnbaum is a strong advocate of transparency and timely communication of the NIEHS's efforts. Through scientific reports, databases, webinars, curricula, presentations, congressional testimonies and briefings, and interagency collaboration, she ensures that our research findings are made available to researchers, regulatory agencies, and the public in formats that are easily accessible and relevant to our stakeholders. Many of these findings have been published in *Environmental Health Perspectives*. Examples of Dr. Birnbaum's influence in this sphere include:

- The NIEHS Translational Research Framework, which includes Partnerships for Environmental Public Health, a program that requires all NIEHS-supported Research Centers to include community engaged activities (https://www.niehs.nih.gov/research/supported/translational/peph/webinars/translational_research_framework/index.cfm).
- Expansion of products for disseminating NTP's scientific work in the form of NTP Technical Reports, evidence maps, and web-based timely releases of NTP study findings.
- Adaptation and application of systematic review methodologies to literature-based evaluations in environmental health.
- Becoming a World Health Organization Collaborating Centre for Environmental Health Sciences, which provides new opportunities for translating research findings into effective

public health interventions to improve health around the world (https://www.niehs.nih.gov/research/programs/geh/partnerships/index.cfm).

Champion of Early Stage Investigators and Training

Dr. Birnbaum has always engaged trainees and students at grantee meetings and university visits. She provided support and encouragement for young scientists and early stage investigators, and she continues to mentor, directly and indirectly, a generation of influential scholars though many different NIEHS-supported mechanisms:

- The CareerTrac trainee tracking system which partners with four Institutes and nearly 35,000 trainees to monitor the career development of trainees. This program was recognized with an NIH Director's Award in 2013.
- The NIEHS Scholars Connect Program which has provided funding for numerous student scholars from underrepresented groups to obtain research training and mentorship at the NIEHS.
- The Outstanding New Environmental Scientist Award which program provides funding support to early stage investigators to conduct cutting-edge research on pressing environmental health problems.

Advocate of Community Engagement

Building on her longstanding commitments to community engagement, environmental public health, and environmental literacy, Dr. Birnbaum instigated and conducted community and virtual forums from Alaska to Anacostia, DC. She has fostered engagement by communities in environmental health research and advocacy across the country by her:

- Encouragement of members of environmental justice communities to work with environmental scientists from around the country to tackle issues in their neighborhoods.
- Commitment to environmental health issues in Native American communities, raising the visibility of the NIEHS and becoming a trusted partner among Tribal Nations.
- Participation in >50 community forums around the country to focus on issues of local concern, such as pollutants in drinking water, impacts of industrial and mining facilities on subsistence lifestyles, and disasters such as the *Deepwater Horizon* oil spill and its impact on human health and local seafood.

Additionally, Dr. Birnbaum encouraged the participation of community members and stakeholders in research funded by the NIEHS. She mandated the establishment of Community Engagement Cores in all NIEHS Centers Programs (e.g., P30, Superfund, Children's Centers, Oceans and Human Health), has been fully supportive and engaged with the Partnerships for Environmental Public Health Program, and has expanded the concepts of environmental health literacy and citizen science. For the past five years, she has sponsored an annual Women's Health Awareness Day that provides health awareness, education, information, resources, and on-site health screenings to local underserved communities.

Proponent of Diversity, Inclusion, Employee Engagement, and Green Management

Within the NIEHS family, Dr. Birnbaum is known for treating everyone with compassion and respect. She established the Office of Science Education and Diversity, created the Institute's first Diversity and Inclusion Strategy, and endorsed anti-harassment education.

Stressing a One NIEHS approach, Dr. Birnbaum promoted collaboration and integration across divisions. For example, she supports "Science Day," which features trans-institute and multidisciplinary research projects. While she maintains high expectations for excellence, Dr. Birnbaum is passionately supportive of all staff maintaining a healthy work/life balance. She expanded health and wellness programs, and encouraged the use of scheduling flexibilities such as alternative work schedules and telework, helping to improve employee engagement and job satisfaction.

Her management of the Institute also reflects her environmental stewardship. Under her leadership, the NIEHS developed its first-ever Sustainability Report, created NIH's first Climate Resiliency Plan, and developed and opened the updated Building 110 Warehouse, the first Net-Zero Energy building in the history of the Department of Health and Human Services. During Dr. Birnbaum's tenure, the Department recognized the NIEHS with 13 Green Champion Awards and 3 Honorable Mentions.

Role Model for Scientific Excellence

Dr. Birnbaum is an internationally recognized and respected authority on the health effects and risk assessment of dioxins and other persistent organic pollutants, such as brominated flame retardants (BFRs). She also pioneered new approaches to assessing developmental toxicity of environmental chemicals, breaking new ground in areas involving a multiplicity of later-life effects, including cancer, reproductive problems, and immune effects. Additionally, her research career has significantly influenced regulatory processes by introducing toxic equivalency factors and body burden as metrics for risk assessment and regulatory decision making.

Dr. Birnbaum has continued to lead her own research laboratory during her time as Director. Over the past 8 years, she has studied the pharmacokinetic and developmental effects of BFRs and examined transcriptomic changes in response to BFRs. She is now moving into work that she began 30 years ago with PFAS. For example, she recently demonstrated that GenX shuts down two major efflux transporters at the rodent blood–brain barrier (P-gp and BCRP) (Cannon et al. 2019) and is now investigating whether this leads to a buildup of compounds in the brain *in vivo*.

Dr. Birnbaum has received many awards and accolades for her leadership and contributions to the field of environmental health sciences. As the 2016 recipient of the State of North Carolina's highest civilian honor, the North Carolina Award, she was praised for her trailblazing work "exploring the effects of dioxins, asbestos, flame retardants and Agent Orange[, which] has impacted practices and health outcomes worldwide" (Lenox 2016). She was elected to the National Academy of Medicine (formerly the Institute of Medicine) of the National Academies of Science, Engineering, and Medicine. She has received the Distinguished Toxicology Scholar Award and the Arnold J. Lehman Award from the Society of Toxicology, as well as the Mildred S. Christian Career Achievement Award from the Academy of Toxicological Sciences. Dr. Birnbaum has also been awarded honorary doctorates from the University of Rochester, the University of Queensland, Ben-Gurion University, and Amity University. Her intramural honors include multiple NIH Director's awards, the NIEHS Champion of Environmental Health Research as part of the NIEHS 50th Anniversary, the Surgeon General's Medallion, and multiple Scientific and Technological Achievement Awards and medals from the U.S. EPA. She was elected into the prestigious Collegium Ramazzini (http://www.collegiumramazzini.org/index.asp) in 2010.

In summary, throughout her long and distinguished career, Dr. Birnbaum has been an innovative and influential researcher and inspirational leader in the areas of environmental exposures,

toxicology, and public health. Although her tenure as the NIEHS and NTP Director is ending, her legacy will live on. The Institute is stronger and more unified than ever, and the science it produces is informing and protecting the public health. Furthermore, the scientists she has trained, influenced, and impacted will carry on her legacy for many years to come. She is a role model for leadership within science, scientific integrity, and appreciation of science as a continuous exploration and source of joy. Dr. Birnbaum leaves a truly distinguished legacy as an environmental health champion.

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